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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/834,110	Applicant(s) PASRICHA ET AL.
	Examiner Joseph Woitach	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7 and 8*
4)☐ Interview Summary (PTO-413) Paper No(s) _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

This application filed April 12, 2001, claims benefit to provisional applications 60/198,806, filed May 13, 2000, and 60/232,301, filed September 12, 2000.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-16, and the species of a degenerative disorder, in Paper No. 10 is acknowledged. The traversal is on the ground(s) that for both the elected invention and the elected species, the inventions as claimed can be readily evaluated in one search and would not impose a serious burden on the Examiner. Applicants arguments have been found persuasive in part. Specifically, upon review of the claims and the teachings in the present disclosure, Examiner agrees that Groups I and II can be examined together without undue burden and the restriction is withdrawn for Groups I and II. However, with respect to the election of species, each of the specific types of disorders have a unique pathology which would require a separate search and consideration for a complete examination of the claimed invention. The search and specific considerations for each disorder would not be co-extensive, and would constitute an undue burden. Therefore, the election of species is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-20 are pending and currently under examination as they are drawn to the treatment of a degenerative disorder.

Drawings

The corrected or substitute drawings were received on August 6, 2001, paper number 5.

Specification

The disclosure is objected to because of the following informalities:

The disclosure contains an embedded hyperlink and/or other form of browser-executable code (see for example page 7; lines 1 and 24, page 8; line 1). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code throughout the specification. See MPEP § 608.01.

Appropriate correction is required.

Claim Objections

Claims 1-20 are objected to because of the following informalities:

The election of species was made to a degenerative disorder, however the claims broadly encompass any disorder. The claims should be amended to reflect the elected invention.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims are drawn broadly to a method of treating a degenerative disorder comprising implanting stem cells or progeny thereof into a gastrointestinal organ. The specification teaches that degenerative disorders is considered broadly to encompass specific diseases associated with the gastrointestinal tract as well as a variety of disorders not traditionally considered gastrointestinal disorders but related to organs associated with the gastrointestinal organs (page 5; lines 15-27). Encompassed within this broad definition diseases such as diabetes, cirrhosis of the liver, as well as other diseases which are associated with the destruction of a particular organ could be treated by the instantly claimed methods. It is noted that the methods simply recite implanting stem cells into a subject, though dependent claims recite specific routes of delivery and delivery to particular organs. The specification provides no working example of the instantly claimed invention as it is drawn to providing treatment or the production of insulin. The only working example presented in the disclosure describes the isolation of a neural stem cell from fetal tissue and transplantation of said cells into the pylorus of the gastrointestinal tract of a mouse. In the working example the neuronal cells differentiate into nitrigenic neurons (page 14). The specification provides only a general summary of a broad range of potential disorders to be

treated and a description of sources of stem cells known in the art at the time of filing. The specification is silent with respect to specific methodology for cell transplantation and provides no guidance for specific treatments of specific disorders except to for the general administration of stem cells for affecting any desired treatment.

The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel*. The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). As noted above, the claims encompass delivery any type of stem cell and treatment of any disorder. More specifically, as directed to the claims specifically claiming the production of insulin several art recognized limitations exist. First, it is well known in the art that a tissue or organ produce and provide environments for growth, development and function which are unique for each specific tissue and organ. With respect to pancreatic progenitor cells, Levine *et al.* teach that human fetal pancreatic cells selected and grown in culture maintain their ability to differentiate into mature endocrine cells following transplantation into the renal capsule of the kidney of a nude mouse (summarized on page 307; abstract and page 311; Table 2). Zayas *et al.* teach similar methods and report that their preparation of human fetal pancreatic progenitor cells maintain the ability to differentiate into fibroblasts and exocrine cells when transplanted into the kidney of a mouse (entire reference and summarized in abstract). As taught in the instant specification, both these references demonstrate that the renal capsule kidney is capable of providing the proper conditions for growth and differentiation of pancreatic progenitor cells.

However, while other tissues may provide the proper environment for growth, not all tissues will support similar differentiation. Dabeva *et al.* teach that "progenitor cells from the pancreas transplanted into the liver will differentiate into hepatocytes, express liver-specific proteins, and become fully integrated into the liver parenchymal structure" (page 7356; abstract). As with most progenitor cells, pancreatic progenitor cells maintain the capacity to differentiate into several different lineages. While the renal capsule of the kidney, and supposedly the pancreas itself, provide a suitable environment for differentiation of pancreatic progenitor cells into more differentiated pancreatic cells, other tissues, such as the liver, will clearly not provide the necessary and proper factors. Applicants have not provided any guidance in the specification nor in the art of record, which demonstrates that they were in possession of the transplantation conditions or specific tissues for the practice of the claimed method in the full scope of the claim.

Secondly, the specification recites only general methodology and provides no means to avoid the hosts immune system which is the major source for graft rejection. No strategies are proposed and it is unclear if these methods would alleviate the graft rejection long enough to accommodate the pancreatic progenitor cell growth and differentiation into more mature cell types and structures to act as a pancreatic model system. In particular, acute graft rejection encountered in xenotransplantation. Mandel teaches that the "current immunosuppression that is usually adequate for control of allograft rejection generally does not prevent xenograft rejection" (page 155; abstract). Further, while current pancreas allograft transplantation are functional at one year (80%), the success rate of isolated cell allograft is poor and "the reasons for this are not

fully understood" (page 155-56; bridging paragraph). Further, Taniguchi *et al.* teach that the host immune response also affected the ability to administer cell therapy when the cells were encapsulated. In attempt to treat hyperglycemia in diabetic mice, encapsulated cells induced an inflammatory response by virtue of the human insulin produced (page 44; bottom of first column). So, while acute rejection of the cell was prevented by encapsulation, the immune response of a foreign antigen, in this case human proinsulin, reduced the ability of the encapsulated cells to serve as a form of cell therapy. Applicants have demonstrated that one can transplant human fetal pancreatic progenitor cells to the renal capsule of the kidney and that said cells can differentiate into cells and structures similar to those seen in a mature pancreas, however, the specification and the art of record demonstrate that there are still several obstacle for the successful xenotransplantation of pancreatic progenitor cells and as a consequence in their ability to provide cell therapy in all circumstances as encompassed by the breadth of the claims, and all of the work required to ultimately develop these methods has been left for others.

The specification fails to provide the necessary guidance to overcome even the specific art recognized limitations for providing insulin. The breadth of the claims is large encompassing any type of stem cell, any means of delivery and affecting treatment for any type of disorder. In view of the quantity of experimentation necessary to determine the parameters listed above for each disorder and/or cell type, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation to affect any treatment, and the general unpredictable state of the art with respect to affecting any treatment, it

would have required undue experimentation for one skilled in the art to make and/or use the claimed inventions as broadly claimed. The specification provides insufficient guidance to teach how to engineer the delivery of insulin to any therapeutic effect in any of the methods proposed.

The high degree of unpredictability associated with a single claimed method underscores the need to provide teachings in the specification that would provide the artisan with specific methodology to practice the full breadth of the claimed invention. In the instant case, the specification does not provide any specific guidance for any specific disease for a therapeutic benefit by a cell based therapy. Further, the specification fails to provide any correlation between routes of delivery (e.g. intratumoral, intravenous etc.), implantation into cells, dosage amounts/frequencies, and specific forms of diseases treatable by the cells comprising such as those disclosed in the instant specification. Without such guidance in the specification the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

The instant invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo*

Nordisk A/S 42 USPQ2d 1001, at 1005). The claimed methods of transfer constitute such a "germ of an idea".

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

Conclusion

No claim is allowed. The claims are free of the art of record because the art fails to teach and enable the breadth of the instantly claimed method. However, the claims are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers

must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Deborah Crouch

Joseph T. Woitach

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630